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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification<sup>6</sup>:</b> <b>C12N 15/30, 15/31, 15/49, A61K 39/39, 39/21</b>		<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 98/01558</b> <b>(43) International Publication Date:</b> <b>15 January 1998 (15.01.98)</b>
<b>(21) International Application Number:</b> <b>PCT/US97/12253</b>		Road, Brookesville, MD 20833 (US). BIRX, Deborah, L. [US/US]; 13 Taft Court #200, Rockville, MD 20850 (US).	
<b>(22) International Filing Date:</b> <b>10 July 1997 (10.07.97)</b>		<b>(74) Agents:</b> WISEMAN, Thomas, G. et al.; Morrison & Foerster LLP, 2000 Pennsylvania Avenue, N.W., Washington, DC 20006-1888 (US).	
<b>(30) Priority Data:</b> 60/021,687	10 July 1996 (10.07.96)	US	<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).
<b>(60) Parent Application or Grant</b> (63) Related by Continuation US Filed on		60/021,687 (CIP) 10 July 1996 (10.07.96)	<b>Published</b> <i>With international search report.</i>
<b>(71) Applicants (for all designated States except US):</b> INTELLIVAX, INC. [US/US]; 6303 Western Run Drive, Baltimore, MD 21215 (US). HENRY M. JACKSON FOUNDATION [US/US]; Suite 600, 1401 Rockville Pike, Rockville, MD 20852 (US). THE GOVERNMENT OF THE UNITED STATES, represented by THE SECRETARY OF THE ARMY [US/US]; 1600 East Grunde Drive, Rockville, MD 20850 (US).		<b>(88) Date of publication of the international search report:</b> <b>14 May 1998 (14.05.98)</b>	

**(54) Title:** PROTEIN AND PEPTIDE VACCINES FOR INDUCING MUCOSAL IMMUNITY**(57) Abstract**

A novel vaccine composition combines a protein or peptide antigen, optionally added hydrophobic material and an immunopotentiating membranous carrier which together preserve the antigenic integrity of the protein or peptide epitopes while at the same time enhancing their immunogenicity. Administration of this composition to a subject provokes a protective immune response comprising secretory neutralizing antibodies present in various mucosal sites in the body. This vaccine and the process for using it is intended for use against pathogenic organisms, in particular those causing sexually transmitted diseases or mucosally transmitted diseases. Such organisms include bacteria and enveloped viruses, particularly HIV-1.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 97/12253

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 C12N15/30 C12N15/31 C12N15/49 A61K39/39 A61K39/21

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbol(s))  
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEVI ET AL: "INTRANASAL IMMUNIZATION OF MICE AGAINST INFLUENZA WITH SYNTHETIC PEPTIDES ANCHORED TO PROTEOSOMES" VACCINE, vol. 13, no. 14, 1995, pages 1353-1359, XP002055656 see the whole document and note especially page 1354, paragraph 3	1,3,4,6, 10-20, 25-32
Y	WO 95 11700 A (PHARMOS CORP ;US GOVERNMENT (US); LOWELL GEORGE H (US); AMSELEM SH) 4 May 1995	2,5,21
X	see page 3, line 32 - page 6, line 15 see page 14, line 13 - page 15, line 9 see page 18 - page 23; examples 1-4	1-4,6-8, 10,11, 13-20, 22,23, 25-32
Y	---	2,5,21
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

13 February 1998

Date of mailing of the international search report

03.03.98

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 97/12253

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LOWELL ET AL: "MUCOSAL IMMUNOGENICITY AND EFFICACY OF PROTEOSOMES AND PA ADJUVANTS FOR HIV, INFLUENZA, SHIGELLA AND STAPH. ENTEROTOXIN B (SEB) VACCINES" JOURNAL OF CELLULAR BIOCHEMISTRY, no. S19A, 1995, page 259 XP002055657 see abstract J1-220	1,2,6-8, 10-12, 16-19, 22,23, 25,26, 30-32
X	KAMINSKI ET AL: "PARENTERAL OR INTRANASAL IMMUNIZATION WITH HIV GP160 FORMULATED WITH PROTEOSOMES AND/OR PA ADJUVANTS ENHANCES EPITOPE-SPECIFIC IGG OR IGA" 94TH GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, 1994, page 155 XP002055658 see abstract E-70	1,2,6-8, 10-12, 16-19, 22,23, 25,26, 30-32
X	LOWELL ET AL: "NASAL IMMUNIZATION WITH HIV GP160 FORMULATED WITH PROTEOSOMES, EMULSOMES AND/OR CHOLERA TOXIN B SUBUNIT: INDUCTION OF ANTI-GP160 SERUM IGA AND IGG AND INTESTINAL, VAGINAL AND LUNG IGA" AMERICAN SOCIETY FOR MICROLBIOLOGY. HUMAN RETROVIRUSES AND RELATED INFECTIONS. 2ND NATIONAL CONFERENCE, - 1995 page 81 XP002055659 see abstract 146	1,2,6-8, 10-12, 16-19, 22,23, 25,26, 30-32
Y	LOWELL ET AL: "PEPTIDES BOUND TO PROTEOSOMES VIA HYDROPHOBIC FEET BECOME HIGHLY IMMUNOGENIC WITHOUT ADJUVANTS" JOURNAL OF EXPERIMENTAL MEDICINE, vol. 167, 1988, pages 658-663, XP002055660 see the whole document	2,5,21
P,X	LOWELL ET AL: "PROTEOSOMES, EMULSOMES, AND CHOLERA TOXIN B IMPROVE NASAL IMMUNOGENICITY OF HUMAN IMMUNODEFICIENCY VIRUS GP160 IN MICE: INDUCTION OF SERUM, INTESTINAL, VAGINAL, AND LUNG IGA AND IGG" THE JOURNAL OF INFECTIOUS DISEASES, vol. 175, no. 2, February 1997, pages 292-301, XP002055661 see page 292 see abstract	1,2,6-8, 10-12, 16-19, 22,23, 25,26, 30-32
1		-/-

## INTERNATIONAL SEARCH REPORT

Int'l. Application No

PCT/US 97/12253

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KAMINSKI ET AL: "HIV PEPTIDE AND PROTEIN ANTIBODY RESPONSES ELICITED BY IMMUNIZATION WITH RGP 160 FORMULATED WITH PROTEOSOMES, ALUM, AND/OR SUBMICRON EMULSIONS" VACCINE RESEARCH, vol. 4, 1995, pages 189-206, XP002055662 see page 189 see abstract ---	
A	LOWELL ET AL: "PROTEOSOME-LIPOPEPTIDE VACCINES: ENHANCEMENT OF IMMUNOGENICITY FOR MALARIA CS PEPTIDES" SCIENCE, vol. 240, 1988, pages 800-802, XP002055663 see page 800 see abstract ---	
A	FRANKENBURG ET AL: "EFFECTIVE IMMUNIZATION OF MICE AGAINST CUTANEOUS LEISHMANIASIS USING AN INTRINSICALLY ADJUVANTED SYNTHETIC LIPOPEPTIDE VACCINE" VACCINE, vol. 14, no. 9, June 1996, pages 923-929, XP002055664 see page 923 see abstract ---	
A	VANCOTT ET AL: "CHARACTERIZATION OF A SOLUBLE, OLIGOMERIC HIV-1 GP160 PROTEIN AS A POTENTIAL IMMUNOGEN" JOURNAL OF IMMUNOLOGICAL METHODS, vol. 183, 1995, pages 103-117, XP002055665 cited in the application see page 103 see abstract ---	
A	YANG ET AL: "THE HUMAN AND SIMIAN IMMUNODEFICIENCY VIRUS ENVELOPE GLYCOPROTEIN TRANSMEMBRANE SUBUNITS ARE PALMITOYLATED" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, USA, vol. 92, 1995, pages 9871-9875, XP002055666 cited in the application see page 9871 see abstract -----	

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 97/12253

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Remark : Although claims 19-32 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l. Application No

PCT/US 97/12253

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9511700 A	04-05-95	AU 5543294 A	22-05-95